

Please add new Claim 58, which is set forth in the enclosed Appendix L.

REMARKS

The response that was filed on February 13, 2003 was completely responsive to the outstanding Office Action that was mailed on August 13, 2002. This supplemental response merely adds some new claims and provides a more detailed explanation why the claimed invention is novel and nonobvious over the prior art.

Hereinafter, the claims that are pending after the entry of the amendments in the February 13, 2003 response and prior to the entry of the amendments in this supplemental response are called "currently pending claims." This supplemental response adds new Claims 39-58. Upon amendment, the above-identified application will have three independent claims (currently pending Claims 1, 31, and 32) and 48 total claims (currently pending Claims 1, 3, 4, 9, 13-15, and 18-38 and new Claims 39-58). The Applicant previously paid for at least three independent claims and 28 total claims. Therefore, a fee is due for 20 additional excess total claims; and a check for this fee is enclosed herewith.

Support for new Claims 39-42 can be found in, inter alia, lines 11-12 on page 10 and lines 8 and 18 on page 32 of the specification.

Support for new Claim 43 can be found in, inter alia, lines 7-8 on page 9 of the specification.

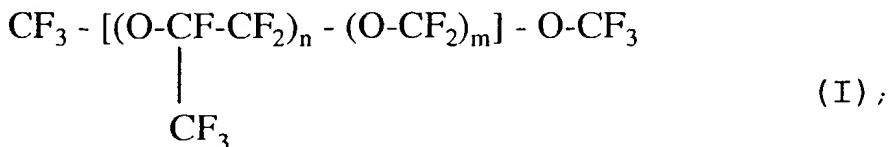
Support for new Claims 44-57 can be found in, *inter alia*, line 11 on page 10 through line 22 on page 57 of the specification.

Support for new Claim 58 can be found in, *inter alia*, originally filed Claim 1 and the table at the top of page 5 of the specification.

In items 4-5 on pages 3-5 of the outstanding Office Action, the Examiner rejects Claims 1, 3, 4, 9, 13-15, 18-28, 31, 32, 34, 35, 37, and 38 for allegedly being obvious over European Patent Publication No. 0390206 A2 (hereinafter referred to as the "Barz document") in view of Gross et al.'s U.S. Patent No. 5,686,102 (hereinafter referred to as the "Gross patent"). The Applicant respectfully traverses this rejection because the prior art does not teach or suggest the claimed invention; and the Applicant also respectfully traverses this rejection for the reasons that are set forth below.

Currently pending Claim 1 claims a pharmaceutical composition comprising:

- (1) one or more pharmacologically active ingredients;
- (2) between 0.01 per cent and 60 per cent by weight of a compound of formula I

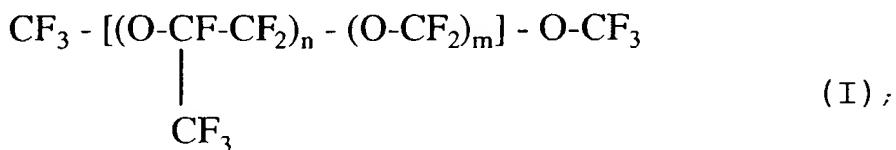


with n and m > 18 and < 46 and with a molecular weight between about 600 and about 8,000; and

- (3) 0.01% to 20% by weight of phosphatidylcholine.

Currently pending independent Claims 31 and 32 each claim a pharmaceutical composition consisting essentially of:

- (1) one or more pharmacologically active ingredients;
- (2) between 0.01 per cent and 60 per cent by weight of a compound of formula I



with n and $m > 18$ and < 46 and with a molecular weight between about 600 and about 8,000;

- (3) phosphatidylcholine; and
- (4) optionally other ingredients.

Currently pending independent Claims 1, 31, and 32 are nonobvious over the prior art because the prior art does not teach or suggest the claimed pharmaceutical composition, which produces superior trans-absorption of the active ingredient (e.g., over 5-20 times the normal trans-absorption) because the claimed pharmaceutical composition includes the compound of formula I and phosphatidylcholine in addition to the pharmacologically active ingredient.

The Barz document discloses a stable emulsion comprising a perfluoropolyether compound of formula I (see line 25 on page 7 of the Barz document), conventional surfactants, and a continuous phase consisting of glycerol or a polyhydroxylated compound containing at least three hydroxyl groups dissolved in a hydrophilic solvent and/or water (see the abstract on page 1 of the Barz document). The resulting stable emulsion forms a water-

repellant and lipo-repellent film that remains on the surface of the skin for a long time and creates a "barrier effect" (see lines 50-53 on page 2 and lines 3-7 on page 3 of the Barz document). In short, Barz's stable emulsion coats the skin, rather than penetrating deeply into the skin.

As noted by the Examiner in the first paragraph on page 4 of the outstanding Office Action, the Barz document does not disclose or suggest using between 0.01% to 20% by weight of phosphatidylcholine, as claimed in amended Claims 1, 31, and 32. Therefore, the Examiner turns to the Gross patent.

The Gross patent (see Claim 1 in column 6) discloses a pharmaceutical composition for topical administration comprising asymmetric lamellar aggregates comprising phospholipids (including phosphatidylcholine), a fluorocarbon, and a pharmacologically active compound, wherein the asymmetric lamellar phospholipid aggregates have a central core of fluorocarbons surrounded by at least three layers of phospholipid molecules, and wherein the layer adjacent to the central core has the lipophilic moiety of the phospholipid interact with the fluorocarbon.

Rather than forming a water-repellant and lipo-repellent film that remains on the surface of the skin for a long time and creates a "barrier effect" like Barz's stable emulsion, Gross's asymmetric lamellar aggregates penetrate deeply through the horny layer of the skin and make the active compound available in the epidermal and dermal region, in the adjoining tissue, or by supplying it to a blood vessel for systemic absorption (see lines 50-55 in column 3 of the Gross patent). The skin-penetrating properties of Gross's asymmetric lamellar aggregates are in sharp contrast to the skin-coating properties of Barz's stable emulsion.

According to the Examiner, it would have been obvious to someone

with ordinary skill in the art to produce the Applicant's claimed pharmaceutical composition by modifying Barz's stable emulsion to include the phosphatidylcholine from Gross's asymmetric lamellar aggregates. However, adding Gross's phosphatidylcholine to Barz's stable emulsion would destroy or impede the stable-emulsive properties of Barz's composition and also would destroy or impede the skin-coating properties of Barz's composition. Given that the purpose of the Barz document is to create a stable emulsion that forms a water-repellant and lipo-repellent film that remains on the surface of the skin for a long time and that creates a "barrier effect" (see lines 50-53 on page 2 and lines 3-7 on page 3 of the Barz document), why would someone with ordinary skill in the art want to add Gross's phosphatidylcholine to Barz's stable emulsion and thereby destroy or impede the stable-emulsive properties and the skin-coating properties of Barz's composition?

The fact that Barz's stable emulsion and Gross's asymmetric lamellar aggregates are both fluorocarbon compositions that are applied to the skin is insufficient to motivate someone with ordinary skill in the art to add Gross's phosphatidylcholine to Barz's stable emulsion because doing so would destroy or impede the very properties that are sought by the Barz document. In fact, the Barz document and the Gross patent are diametrically opposed to each other and teach away from each other because the Barz document discloses a stable emulsion that sits on the surface of the skin, while the Gross patent discloses asymmetric lamellar aggregates that penetrate deeply through the horny layer of the skin, rather than sitting on the surface of the skin. Destroying or impeding the stable-emulsive properties and the skin-coating properties of Barz's composition is contrary to the teachings of the Barz document; and nothing in the prior art would motivate someone with ordinary skill to contravene the teachings of the Barz document by adding Gross's phosphatidylcholine to Barz's stable emulsion in order to destroy or impede the Barz

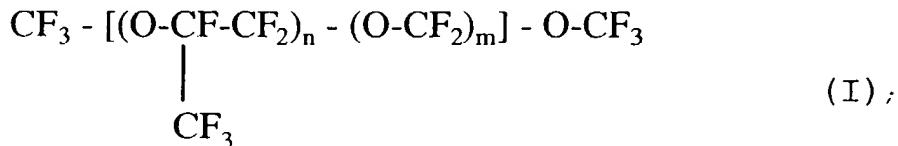
composition's stable-emulsive properties and skin-coating properties.

The Barz document teaches away from the Gross patent because the skin-coating properties of Barz's stable emulsion are diametrically opposed to the skin-penetrating properties of Gross's asymmetric lamellar aggregates; and only someone who has read the Applicant's above-identified U.S. application with 20/20 hindsight would be motivated to add Gross's phosphatidylcholine to Barz's stable emulsion and thereby destroy or impede the stable-emulsive properties and the skin-coating properties of Barz's composition. By contrast, someone who has read the prior art without first reading the Applicant's above-identified U.S. application would not be motivated to add Gross's phosphatidylcholine to Barz's stable emulsion because doing so would destroy or impede the Barz composition's stable-emulsive properties and skin-coating properties, which are the very properties that are sought by the Barz document.

In summary, currently pending independent Claims 1, 31, and 32 are nonobvious over the Barz document in view of the Gross patent because the Barz document teaches away from the Gross patent, and because someone with ordinary skill in the art who has not read the Applicant's above-identified U.S. application would not be motivated to add Gross's phosphatidylcholine to Barz's stable emulsion since doing so would destroy or impede the Barz composition's stable-emulsive properties and skin-coating properties, which are the very properties that are sought by the Barz document. In short, currently pending independent Claims 1, 31, and 32 are nonobvious over the prior art because the prior art does not teach or suggest the claimed pharmaceutical composition, which includes the compound of formula I, phosphatidylcholine, and a pharmacologically active ingredient.

Currently pending independent Claims 31 and 32 are further nonobvious over the Barz document in view of the Gross patent for the following reasons. As noted above, currently pending Claims 31 and 32 each claim a pharmaceutical composition consisting essentially of:

- (1) one or more pharmacologically active ingredients;
- (2) between 0.01 per cent and 60 per cent by weight of a compound of formula I



with n and m > 18 and < 46 and with a molecular weight between about 600 and about 8,000;

- (3) phosphatidylcholine; and
- (4) optionally other ingredients.

Currently pending Claims 31 and 32 have been drafted to specifically exclude ingredients that are required by the Barz document. As explained above, the Barz document discloses a stable emulsion comprising a perfluoropolyether compound of formula I (see line 25 on page 7 of the Barz document), conventional surfactants, and a continuous phase consisting of glycerol or a polyhydroxylated compound containing at least three hydroxyl groups dissolved in a hydrophilic solvent and/or water (see the abstract on page 1 of the Barz document). There is no teaching or suggestion in the prior art (e.g., in the Barz document or the Gross patent) that this "continuous phase" is optional because this "continuous phase" is needed to produce Barz's stable emulsion and, more particularly, is needed to

produce the stable-emulsive properties and the skin-coating properties that are characteristic of Barz's composition. By contrast, currently pending Claims 31 and 32 exclude the "continuous phase" that is disclosed in the Barz document because the Applicant does not seek the stable-emulsive properties and the skin-coating properties that are characteristic of Barz's composition. And because currently pending Claims 31 and 32 specifically exclude the "continuous phase" that is required by the Barz document, currently pending independent Claims 31 and 32 are further nonobvious over the prior art (i.e., currently pending independent Claims 31 and 32 are further nonobvious over the Barz document in view of the Gross patent).

For the foregoing reasons, currently pending independent Claims 1, 31, and 32 are nonobvious over the prior art. All of the other claims (i.e., currently pending Subclaims 3, 4, 9, 13-15, 18-30, and 32-38, and new Subclaims 39-58) are nonobvious over the prior art at the very least because they are each directly or indirectly dependent on a nonobvious base claim. In addition, these subclaims are further nonobvious over the prior art because the prior art does not teach or suggest the particular features that are claimed in these subclaims. For example, new Subclaims 39-42, 44-55, and 57 are further nonobvious over the prior art because they each claim pharmaceutical compositions comprising pharmacologically active ingredients that are not disclosed or suggested by the prior art (e.g., the Gross patent and the Barz document).

The Applicants are pleased to note that currently pending Claims 29, 30, 33, and 36 contain allowable subject matter according to item 6 on page 6 of the outstanding Office Action.

In view of the foregoing, favorable reconsideration of the amended application is respectfully requested. It is submitted that the

claims of record are in condition for allowance. Allowance of the claims at an early date is solicited.

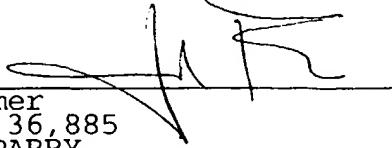
This supplemental response adds new Claims 39-58. The additions that are described in the preceding sentence were done to more fully claim the Applicant's invention and were not done to overcome the prior art, were not done to overcome rejections under 35 U.S.C. § 112, and were not done to overcome any other rejections or objections. The additions that are described in the first sentence of this paragraph shall not be considered necessary to overcome the prior art, shall not be considered necessary to overcome rejections under 35 U.S.C. § 112, and shall not be considered necessary to overcome any other rejections or objections.

The Applicant reserves the right to seek protection for any unclaimed subject matter either subsequently in the prosecution of the present case or in a divisional or continuation application.

The Commissioner is authorized to charge any additional fees which may be required or credit overpayment to Deposit Account No. 12-0415. In particular, if this response is not timely filed, then the Commissioner is authorized to treat this response as including a petition to extend the time period pursuant to 37 C.F.R § 1.136(a) requesting an extension of time of the number of months

necessary to make this response timely filed; and the petition fee due in connection therewith may be charged to deposit account No. 12-0415.

Respectfully submitted,


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Enclosures: Appendices J, K, and L